Remarks/Arguments

This is in response to the outstanding Office Action mailed September 11, 2003, and is accompanied by a petition for a three month extension of time. The last day of the response period is March 11, 2004.

Claims 1-3, 7-12 and 70 are pending in the application. Claims 1, 7-12 and 70 have been rejected, whereas Claims 2 and 3 are objected to. Without prejudice as to further prosecution, Claims 8, 9, and 70 are hereby amended. Applicant reserves the right to present canceled subject matter in a continuation application. Claims 81-91 are new. Claims 83 and 84 are, respectively, Claims 2 and 3 written in independent form. Claims 85-91 are similar to Claims 7-12, and 70 but dependent on Claims 83 and 84.

First Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1, 7-12 and 70 stand rejected under § 112, first paragraph as containing subject matter that is not described in such a was as to convey that the inventors had possession of the claimed invention. This rejection is respectfully traversed.

Applicants respectfully assert that the Examiner has not met the burden of presenting evidence that shows why one of ordinary skill in the art would not recognize that the written description of the instant invention supports the claims.

If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. *See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); Martin v. Johnson, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972)* (stating "the description need not be ipsis verbis to be sufficient")

Here, the structural and functional characteristics of wth3 nucleic acids and proteins fully describe the subject matter encompassed by the claims. Aside from the disclosed wth3 protein and nucleic acid sequences and protein family homology, the Applicants have disclosed the genetic locus of wth3. The genetic locus is a structural characteristic which defines wth3, and in particular, describes variants such as allelic, polymorphic or splice

variants as have been raised by the Examiner. The specification goes further, and points out functional characteristics of the wth3 gene and protein, correlating its underexpression with multiple drug resistance and disclosing that drug sensitivity is enhanced in cells in which an exogenous source of wth3 is provided. Applicants further disclose that overexpression of a wth3 homolog (*e.g.*, rab6, rab6c) also enhances drug sensitivity.

Accordingly, it is asserted that Applicants have satisfied the written description requirement by describing a combination of identifying characteristics sufficient to show possession of the claimed invention. Applicants have disclosed structural and biochemical properties of wth3 proteins and nucleic acids, as well as homologs of wth3, and further, that the disclosed structural and biochemical properties establish a correlation between function and structure for the claimed subject matter.

The Examiner has cited disparate references, and referred to specific propositions in those references in isolation from other considerations that would be apparent to one of ordinary skill in the art. The Examiner has cited the Glossary of Genetics to point out possible functional differences among different allelic proteins. However, the Applicants invention is not described solely in terms of protein function, but also in terms of chromosomal location, expression pattern of the encoding nucleic acids, and structural and functional homology within a family of proteins.

One of ordinary skill would appreciate the possibility of functional variation among wth3 alleles and still be able to recognize the claimed invention, relying also on any one or more of the additional attributes disclosed in the specification which describe wth3. Those attributes include structural attributes such as chromosomal location which, as taught by The Glossary of Genetics and the art, is the location at which an allelic variant is found. Applicant's defined chromosomal location for wth3 is a structural characteristic that is common to <u>all</u> wth3 alleles. Other disclosed attributes are the length of the coding sequence, the size of the transcript, hypomethylation in multiple drug resistant cells, and the inverse relationship between gene expression and multiple drug resistance. Further, the specification sets forth the structure of the wth3 gene with respect to other conserved rab6 family members, showing the regions where the nucleic acids and proteins are similar or divergent

(See Figs. 1-4), and establishes common biochemical properties with respect to multidrug resistance.

Similarly, the Examiner has cited Bork and Koonin for the proposition that homologs in different species may not have the same functional characteristics. However, upon close examination, the material that is specifically cited by the Examiner (page 315, second column, lines 11-16 under the heading "Effects of noise on function predictions") relates to functional predictions based on sequence homology. The authors are saying that in trying to predict the function of a newly discovered sequence, there is no automatic means to establish how much functional information obtained from a homolog in a database can also be attributed to the newly discovered sequence of otherwise unknown function.

In contrast, Applicants disclose actual functional characteristics without resorting to prediction. Applicants have not only disclosed wth3 sequences in structural terms, but have also functionally characterized wth3 in terms of observable and measurable physiological effects. Applicants have not relied on homology to other proteins or nucleic acids to determine a function of wth3. Rather, having established that function, the Applicants showed that rab6 family members that are homologous to wth3 possessed similar properties. One of ordinary skill in the art would recognize which nucleic acids and encoded proteins are claimed on the basis of homology and function. If those of ordinary skill have any question as to the identities or functions of homologs genes or proteins, they need simply test for characteristics that Applicants teach for wth3. For example, in addition to sequence homology, a gene encoding a homolog in another species would be hypomethylated in multiple drug resistant cells. Also, the homolog, when overexpressed in a cell, would increase the sensitivity of the cell to drugs such as doxorubicin and other chemotherapeutics.

Accordingly, it is again respectfully asserted that there is no reasonable basis for one of ordinary skill in the art to conclude that Applicants were not in possession of the claimed subject matter. Applicant respectfully requests that the first rejection under 35 U.S.C. §112, first paragraph be withdrawn.

Second Rejection Under 35 U.S.C. § 112, first paragraph

Claims 11 and 12 were rejected under 35 U.S.C. § 112, first paragraph for lack of an enabling disclosure. It is believed that the rejection is rendered moot by the amendment to Claim 9. Withdrawal of the second rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

Rejection Under 35 U.S.C. § 101

Claims 7-9, and 70 are rejected under 35 U.S.C. § 101, as directed to non-statutory subject matter. It is believed that the rejection is rendered moot by the claim amendments. Withdrawal of the rejection under 35 U.S.C. §101 is respectfully requested.

Conclusion

It is believed that this amendment is fully responsive to the outstanding Office Action, and favorable action is respectfully requested. If a telephone conversation would further the prosecution of the present application, the Examiner is invited to contact the undersigned to resolve any issues that might remain.

Respectfully submitted,

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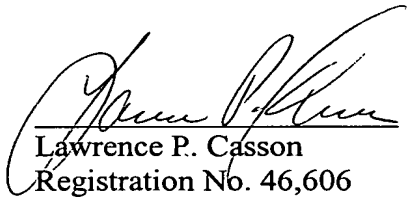
Date: March 11, 2004 By: 

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